What is claimed is:

1. A method for treating diabetes, the method comprising administering to a mammal in need thereof a therapeutically effective amount of a composition comprising a gastrin /CCK receptor ligand and a factor for complementing gastrin for islet neogenesis therapy (a FACGINT), provided that the FACGINT is not an EGF receptor ligand.

2. A method according to claim 1, wherein the FACGINT is at least one selected from the group of: a Glucagon-like peptide 1 receptor ligand; a Glucagon-like peptide 2 receptor ligand; a gastric inhibitory polypeptide (GIP) receptor ligand; a keratinocyte growth factor (KGF) receptor ligand; a dipeptidyl peptidase IV inhibitor; a REG protein receptor ligand; a Growth Hormone receptor ligand; a Prolactin (PRL) receptor ligand ; an Insulin-like Growth Factor (IGF) receptor ligand; PTH-related protein (PTHrP) receptor ligand; hepatocyte growth factor (HGF) receptor ligand; a bone morphogenetic protein (BMP) receptor ligand, a transforming growth factor-β (TGF-β) receptor ligand; a laminin receptor ligand; vasoactive intestinal peptide (VIP) receptor ligand; a fibroblast growth factor (FGF) receptor ligand; a keratinocyte growth factor receptor ligand; a nerve growth factor (NGF) receptor ligand; an islet neogenesis associated protein (INGAP) receptor ligand; an Activin-A receptor ligand; a vascular endothelial growth factor (VEGF) receptor ligand; an erythropoietin (EPO) receptor ligand; a pituitary adenylate cyclase activating polypeptide (PACAP) receptor ligand; a granulocyte colony stimulating factor (G-CSF) receptor ligand; a granulocyte-macrophage colony stimulating factor (GM-CSF); a platelet-derived growth factor (PDGF) receptor ligand; and a Secretin receptor ligand.

3. A method according to claim 1, wherein the FACGINT comprises a Glucagon 1-like peptide receptor ligand which is a GLP-1 or exendin-4.

4. A method according to claim 2, wherein the FACGINT comprises a Growth Hormone receptor ligand comprising a Growth Hormone.

5. A method for treating diabetes, the method comprising:

contacting *ex vivo* a plurality of cells with a composition comprising at least one FACGINT and a gastrin/CCK receptor ligand, provided that the FACGINT is not an EGF receptor ligand; and

administering the cells to a mammal in need thereof, thereby treating the diabetes.

6. The method according to claim 5, wherein the cells are autologous.

7. The method according to either of claims 1 or 5, wherein administering or contacting is providing the composition in an amount effective to increase the amount of insulin secreting cells in the mammal.

8. The method according to either of claims 1 or 5, wherein the composition is administered systemically.

9. The method according to either of claims 1 or 5, wherein the amount of the FACGINT in the composition is substantially less than the minimum effective dose of the FACGINT required to reduce blood glucose in the diabetic mammal in the absence of a gastrin/CCK receptor ligand

10. The method according to either of claims 1 or 5, further comprising measuring a parameter selected from the group of: blood glucose, serum glucose, blood glycosylated hemoglobin, pancreatic β cell mass, serum insulin, pancreatic insulin content, and morphometrically determined β cell mass.

11. The method according to claim 5, wherein the cells are pancreatic ductal cells.

12. The method according to claim 1, further comprising measuring a parameter selected from the group of: amount of insulin secreting cells, glucose responsiveness of insulating secreting cells, amount of proliferation of islet precursor cells, and amount of mature insulin secreting cells.

13. A method for inducing pancreatic islet neogenesis in a mammal, the method comprising administering to the mammal a composition comprising a combination of a FACGINT and a gastrin /CCK receptor ligand provided that the FACGINT is not an EGF receptor ligand, in an amount sufficient to increase proliferation of islet precursor cells in pancreatic tissue, thereby inducing pancreatic islet neogenesis.

14. A method for inducing pancreatic islet neogenesis in a mammal, the method comprising administering a composition comprising a combination of a FACGINT and a gastrin /CCK receptor ligand wherein the FACGINT is not an EGF receptor ligand, in an amount sufficient to increase the number of pancreatic insulin secreting β cells in the mammal.

15. The method according to claim 5, further comprising prior to the contacting step, culturing the cells *ex vivo*.

16. A composition comprising a gastrin/CCK receptor ligand and a FACGINT, provided that the FACGINT is not an EGF receptor ligand.

17. The composition according to claim 16 in a dosage effective for inducing differentiation of an islet precursor cell into a mature insulin secreting cell.

18. The composition according to claim 16 in a pharmaceutically acceptable carrier.

19. A kit for treating or preventing diabetes, containing a composition comprising a gastrin/CCK receptor ligand and a FACGINT, a container, and instructions for use, provided that the FACGINT is not an EGF receptor ligand.

20. The kit according to claim 19, wherein the composition further comprises a pharmaceutically acceptable carrier.

21. A method for expanding and differentiating stem cells into insulin secreting cells in a diabetic recipient of implanted cells, comprising implanting the stem cells in the recipient, and administering to the recipient a composition containing an effective dose of each of a gastrin/CCK receptor ligand and at least one FACGINT provided that the FACGINT is not an EGF receptor ligand.

22. The method according to claim 21, wherein the cells are obtained from a human or a porcine.

23. The method according to claim 21, wherein the implanted cells are obtained from pancreatic islets, umbilical chords, embryos, or stem cell lines.

24. A method according to any of claims 1, 5, 13, 14 and 21, wherein the gastrin/CCK receptor ligand is gastrin.

25. A method according to claim 24, wherein the gastrin is gastrin-17.

26. The method according to claim 24, wherein the gastrin/CCK receptor ligand is human gastrin 1-17Leu15.

27. The method according to claim 23, wherein implanting the cells in the recipient is using a route selected from: injecting directly into an organ, and administering intravenously.

28. The method according to claim 23, wherein administering the cells is delivering locally into an organ selected from the pancreas, the kidney, and the liver.

29. The method according to claim 28, wherein delivering the cells locally is a step selected from the group consisting of: endoscopic retrograde cholangiopancreatography (ERCP); endoscopic ultrasound-guided fine needle delivery (EUS-FNAD); injection into a pancreatic artery; injection into a portal vein; intrapancreatic injection; and injection into an hepatic artery.

30. The method according to claim 27, wherein injecting the cells is delivering to the portal vein percutaneously or transhepatically.

31. The method according to claim 23, further comprising prior to the implanting step, treating the cells *ex vivo* with the composition.

32. A method for reducing an amount of stem cells needed for transplantation to treat human diabetes, the method comprising administering to the recipient an effective dose of each of a gastrin/CCK receptor ligand and a FACGINT provided that the FACGINT is not an EGF receptor ligand, wherein the amount of cells needed is reduced in comparison to an amount of cells needed in the absence of administering the effective dose to an otherwise identical recipient.

33. The method according to either of claims 1 and 2, further comprising administering to the subject an agent for suppressing an immune response.

34. The method according to claim 33, wherein the agent for suppressing immune response is a drug.

35. The method according to claim 32, wherein the agent for suppressing immune response is selected from at least one of the group consisting of a rapamycin; a corticosteroid; an azathioprine; mycophenolate mofetil; a cyclosporine; a cyclophosphamide; a methotrexate; a 6-mercaptopurine; FK506; 15-deoxyspergualin; an FTY 720; a mitoxantrone; a 2-amino-1,3-propanediol; a 2-amino-2[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride; a 6-(3-dimethyl-aminopropionyl) forskolin; and a demethimmunomycin.

36. The method according to claim 32, wherein the agent for suppressing immune response is a protein.

37. The method according to claim 36, wherein the protein comprises an amino acid sequence of an antibody.

38. The method according to claim 37, wherein the agent for suppressing immune response is selected from the group consisting of at least one of: hul 124; BTI-322; allotrap-HLA-B270; OKT4A; Enlimomab; ABX-CBL; OKT3; ATGAM; basiliximab; daclizumab; thymoglobulin; ISAtx247; Medi-500; Medi-507; Alefacept; efalizumab; infliximab; and an interferon.

39. The method according to claim 32, wherein the islet neogenesis therapy composition and the agent for suppressing immune response are administered sequentially.

40. The method according to claim 32, wherein at least one of the islet neogenesis therapy composition and the agent for suppressing immune response is administered systemically.

41. The method according to claim 40, wherein the islet neogenesis therapy composition is administered as a bolus.

42. The method according to claim 32, wherein at least one of the islet neogenesis therapy composition and the agent for suppressing immune response is administered by a route selected from the group consisting of intravenous, subcutaneous, intraperitoneal, and intramuscular.

43. The method according to claim 32, wherein the agent for suppressing immune response is administered orally.

44. The method according to claim 32, wherein the agent for suppressing immune response is at least one selected from the group of FK506, rapamycin, and daclizumab.

45. The method of according to either of claims 1 or 32, wherein the subject is a human.

46. A kit for treatment of a diabetic subject, comprising an immunosuppressive agent, an INT composition comprising a FACGINT provided that the FACGINT is not an EGF receptor ligand, and a container.

47. A pharmaceutical composition comprising a FACGINT provided that the FACGINT is not an EGF receptor ligand and an agent for immune suppression.

48. A pharmaceutical composition for sustained release of an I.N.T.™ therapeutic composition, the composition comprising: a gastrin receptor ligand; and an EGF receptor ligand or a FACGINT; wherein at least one of the gastrin receptor ligand, or the EGF receptor ligand or FACGINT, is a sustained release formulation.

49. The composition according to either of claims 16 and 48, further comprising an agent for immune suppression.

50. The composition according to claim 48, wherein the sustained release formulation is selected from the group consisting of pegylation and a multivesicular lipid-based liposome.

51. The composition according to claim 48, wherein the EGF receptor ligand is selected from the group consisting of an EGF and a TGFA.

52. A composition according to claim 48, wherein the FACGINT is at least one selected from the group of: a Glucagon-like peptide 1 receptor ligand; a Glucagon-like

peptide 2 receptor ligand; a gastric inhibitory polypeptide (GIP) receptor ligand; a keratinocyte growth factor (KGF) receptor ligand; a dipeptidyl peptidase IV inhibitor; a REG protein receptor ligand; a Growth Hormone receptor ligand; a Prolactin (PRL) receptor ligand ; an Insulin-like Growth Factor (IGF) receptor ligand; PTH-related protein (PTHrP) receptor ligand; hepatocyte growth factor (HGF) receptor ligand; a bone morphogenetic protein (BMP) receptor ligand, a transforming growth factor-β (TGF-β) receptor ligand; a laminin receptor ligand; vasoactive intestinal peptide (VIP) receptor ligand; a fibroblast growth factor (FGF) receptor ligand; a keratinocyte growth factor receptor ligand; a nerve growth factor (NGF) receptor ligand; an islet neogenesis associated protein (INGAP) receptor ligand; an Activin-A receptor ligand; a vascular endothelial growth factor (VEGF) receptor ligand; an erythropoietin (EPO) receptor ligand; a pituitary adenylate cyclase activating polypeptide (PACAP) receptor ligand; a granulocyte colony stimulating factor (G-CSF) receptor ligand; a granulocyte-macrophage colony stimulating factor (GM-CSF); a platelet-derived growth factor (PDGF) receptor ligand; and a Secretin receptor ligand.

53. The composition according to claim 51, wherein the EGF receptor ligand is a low molecular weight drug.

54. The composition according to claim 48, formulated for parenteral administration.

55. The composition according to claim 48, formulated for oral administration.

56. The composition according to claim 50, formulated for a route of administration selected from the group consisting of subcutaneous, intraperitoneal, intravenous, and intramuscular injection.

57. The composition according to claim 48, wherein at least one of the gastrin receptor ligand, or the EGF receptor ligand or the FACGINT, is formulated for systemic administration.

58. The composition according to any of claims 16 and 48, formulated for local delivery.

59. The composition according to claim 58, wherein local delivery is targeted to the pancreas.

60. The composition according to claim 58, wherein local delivery is selected from the group consisting of: endoscopic retrograde cholangiopancreatography (ERCP); endoscopic ultrasound-guided fine needle aspiration delivery (EUS-FNAD); injection into a

pancreatic artery; injection into a portal vein; intrapancreatic injection; and injection into an hepatic artery.

61. The composition according to any of claims 16 and 48, formulated for a route of administration selected from the group consisting of transdermal and mucosal delivery.

62. The pharmaceutical composition according to claim 48, formulated for delivery by a mechanical device.

63. The composition according to any of claims 16 and 48, formulated for administration with a device selected from the group of: a degradable implant; a transcutaneous patch; a catheter; an implantable pump; a percutaneous pump; an infusion pump; and an iontophoresis device.

64. The pharmaceutical composition according to claim 48, formulated for a route of administration selected from the group consisting of: subcutaneous, intraperitoneal, intravenous, and intrapancreatic.

65. The pharmaceutical composition according to claim 64, wherein the intravenous route is into a portal vein.

66. The pharmaceutical composition according to claim 62, wherein the device is a pump.

67. The pharmaceutical composition according to claim 62, wherein the administration is local.

68. The composition according to claim 48, wherein the administration is local and is delivered by a route selected from the group of: endoscopic retrograde cholangiopancreatography (ERCP); endoscopic ultrasound-guided fine needle aspiration delivery (EUS-FNAD); injection into a pancreatic artery; injection into a portal vein; intrapancreatic injection; and injection into an hepatic artery

69. The pharmaceutical composition according to claim 62, wherein the administration is systemic.

70. The pharmaceutical composition according to claim 48, in an effective dose.

71. A kit comprising at least one dose of a composition according to claim 48.

72. A method of reducing frequency of treating a diabetic subject with an I.N.T.™ composition, the method comprising:

preparing at least one component of the composition as a sustained release formulation; and

administering the composition to the subject according to a protocol having greater intervals between treatments than for the composition not so formulated and otherwise identical.

73. The method according to claim 72, wherein administering is delivering by a route selected from: endoscopic retrograde cholangiopancreatography (ERCP); endoscopic ultrasound-guided fine needle aspiration delivery (EUS-FNAD; injection into a pancreatic artery; injection into a portal vein; intrapancreatic injection; and injection into an hepatic artery.

74. A method of enhancing efficacy of an I.N.T.™ composition in a diabetic subject, the method comprising:

administering to the subject an I.N.T.™ composition having at least one component of the composition formulated to produce a sustained release; and

comparing efficacy in treating the subject of an amount of the composition administered to efficacy of a composition not having a component so formulated and otherwise identical, such that the efficacy of the I.N.T.™ composition having a sustained release formulated composition, as measured by a decrease in an amount of the sustained release formulated agent required to reduce or eliminate symptoms of diabetes in the subject, is enhanced.

75. The method of claim 74, wherein comparing efficacy is further analyzing toxicity of the composition, such that fewer or milder unwanted symptoms following administering the composition indicates decreased toxicity in the composition having at least one component formulated to produce a sustained release, compared to toxicity of the I.N.T.™ composition not having a component so formulated and otherwise identical.

76. The method according to any of claims 73-75, wherein the sustained release formulation of the component is selected from the group consisting of pegylation and a multivesicular lipid-based liposome.

77. The method according to any according to any of claims 73-76, wherein the component having the sustained release formulation is an EGF receptor ligand selected from the group consisting of an EGF and a TGFα.

78. The method according to any of claims 73-76, wherein the FACGINT is at least one selected from the group of: a Glucagon-like peptide 1 receptor ligand; a Glucagon-like peptide 2 receptor ligand; a gastric inhibitory polypeptide (GIP) receptor ligand; a keratinocyte growth factor (KGF) receptor ligand; a dipeptidyl peptidase IV inhibitor; a REG

protein receptor ligand; a Growth Hormone receptor ligand; a Prolactin (PRL) receptor ligand ; an Insulin-like Growth Factor (IGF) receptor ligand; PTH-related protein (PTHrP) receptor ligand; hepatocyte growth factor (HGF) receptor ligand; a bone morphogenetic protein (BMP) reeceptor ligand, a transforming growth factor-β (TGF-β) receptor ligand; a laminin receptor ligand; vasoactive intestinal peptide (VIP) receptor ligand; a fibroblast growth factor (FGF) receptor ligand; a keratinocyte growth factor receptor ligand; a nerve growth factor (NGF) receptor ligand; an islet neogenesis associated protein (INGAP) receptor ligand; an Activin-A receptor ligand; a vascular endothelial growth factor (VEGF) receptor ligand; an erythropoietin (EPO) receptor ligand; a pituitary adenylate cyclase activating polypeptide (PACAP) receptor ligand; a granulocyte colony stimulating factor (G-CSF) receptor ligand; a granulocyte-macrophage colony stimulating factor (GM-CSF); a platelet-derived growth factor (PDGF) receptor ligand; and a Secretin receptor ligand.

79. The method according to claim 78, wherein the component is a low molecular weight drug.

80. The method according to any of claims 73-76, wherein administering is delivering by a route selected from the group consisting of parenteral, oral, transdermal, subcutaneous, mucosal, intraperitoneal, intravenous, intrapancreatic and intramuscular.

81. The method according to claim 80, wherein administering produces local distribution.

82. The method according to claim 82, further comprising administering the composition in an effective dose.

83. The method according to claim 80, wherein prior to administering, the composition is formulated for using a sustained release device.

84. The method according to claim 83, wherein the device selected from the group of: degradable implant; transcutaneous patch; catheter; implantable pump; percutaneous pump; infusion pump; and iontophoresis device.

85. The method according to claim 84, wherein the device is a pump.

86. The method according to claim 80, wherein administering by the intravenous route is injecting into a portal vein.

87. A method of reducing frequency of treating a diabetic subject, the method comprising preparing a device for administering an I.N.T.^{TM} composition to the subject by continuous release for a prolonged period; providing the device to the subject; and re-iterating treating the subject by replacing or refilling the device.

88. A method according to claim 87, wherein the device is a pump.

89. A method according to claim 88, wherein the pump is selected from the group consisting of: a percutaneous pump; a flurorcarbon propellant pump; an osmotic pump; a mini-osmotic pump; an implantable pump; and an infusion pump.

90. A method according to claim 87, wherein the device is selected from the group consisting of: a degradable implant; a non-degradable implant; a mucoadhesive implant; a transcutaneous patch; a catheter; and an iontophoresis device.

91. A method for expanding and differentiating stem cells into insulin secreting cells in a diabetic recipient of the cells, comprising:

implanting the cells in the recipient; and

administering a sustained release composition comprising an effective dose of each of: a gastrin/CCK receptor ligand; and a FACGINT or an EGF receptor ligand, wherein the stem cells are expanded and differentiated into insulin secreting cells in the recipient.

92. A composition for treating diabetes comprising a Glucagon-like peptide–1 (GLP-1) receptor ligand and a gastrin/CCK receptor ligand.

93. The composition according to claim 92, wherein the GLP-1 receptor ligand is GLP-1.

94. A composition for treating diabetes comprising a Growth Hormone (GH) receptor ligand and a gastrin/CCK receptor ligand.

95. The composition according to claim 94, wherein the GH is human growth hormone (HGH).

96. A composition for treating diabetes comprising a prolactin (PL) receptor ligand and a gastrin/CCK receptor ligand.

97. The composition according to claim 96, wherein the PL is human PL.

98. The compositions according to any of claims 92-97, wherein the gastrin is gastrin I having 17 amino acids with a Leu residue at amino acid position 15.

99. The compositions according to any of claims 92-98, further comprising an agent for immune suppression.

100. The compositions according to any of claim 92-99, further formulated for sustained release.

101. A method of treating a diabetic subject comprising administering to the subject a composition comprising a gastrin /CCK receptor ligand and a Glucagon-like peptide–1 (GLP-1) receptor ligand.

102. A method of treating a diabetic subject comprising administering to the subject a composition comprising a gastrin /CCK receptor ligand and a Growth Hormone (GH) receptor ligand.

103. A method of treating a diabetic subject comprising administering to the subject a composition comprising a gastrin /CCK receptor ligand and a prolactin (PL) receptor ligand.

104. The methods of any of claims 101-103 further comprising administering an agent for immune suppression.

105. The methods of any of claims 101-104 further comprising administering at least one of the receptor ligands or agents using a sustained release device.

106. The methods of any of claims 101-104 further comprising formulating at least one of the receptor ligands or agents for sustained release.

107. The methods of any of claims 101-104 wherein the diabetic subject has type I diabetes or type II diabetes.

108. A method for expanding a functional β cell mass of pancreatic islet transplants in a diabetic patient recipient of a transplant of purified islets, the method comprising administering to the mammal an effective dose of a gastrinCCK receptor ligand and a FACGINT.

109. A method of treating human diabetes comprising transplanting a pancreatic islet preparation into a diabetic patient; and administering to the patient an effective dose of a gastrin/CCK receptor ligand and a FACGINT.

110. A method according to claim 1, wherein the FACGINT comprises a prolactin receptor ligand which is prolactin.